PATENT COOPERATION TREATY

PC

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	07.09.2001
Applicant's or agent's file reference PC/SJB/P10758PC	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/02414	21/06/2000	21/06/1999

Applicant
UNIVERSITY COURT OF THE UNIVERSITY OF DUNDEE et al

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Exner, K Tel.+49 89 2399-7826

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
PC/SJB/P10758PC		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/02414	21/06/2000	21/06/1999
International Patent Classification (IPC) or national classification and IPC C07K14/47		
Applicant UNIVERSITY COURT OF THE UNIVERSITY OF DUNDEE et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
22/12/2000	07.09.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Schnack, A Telephone No. +49 89 2399 8149

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/02414

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-30 as originally filed

Claims, No.:

1-5 as received on 27/07/2001 with letter of 27/07/2001

Drawings, sheets:

1/12-12/12 as originally filed

Sequence listing part of the description, pages:

1-3, filed with the letter of 13.11.00

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☒ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☒ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)
   see separate sheet

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-4
	No:	Claims	none
Inventive step (IS)	Yes:	Claims	none
	No:	Claims	1-4
Industrial applicability (IA)	Yes:	Claims	1-4
	No:	Claims	none

2. Citations and explanations
   see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Reference is made to the following documents:

D4: Proceedings of the American Association for Cancer Research annual, vol. 38, 1997, p. 624.

D5: TIBS Trends in Biochemical Science, vol. 22, no. 9, 1997, pp. 345-349.

D6: The EMBO Journal, vol. 16, no. 5, 1997, pp. 1114-1121.

Section I
Basis

Support in the sense of Rule 70.2(c) PCT cannot be found for the subject matter according to present claim 5. Thus, the subject matter according to this claim has not be examined.

Section V
V.1. Novelty
Remarks under Article 33(2) PCT:

D5 disclose the sequence (K/R)xxYDRxFL(L/M) as the binding site for eIF4E-binding, (see D5, page 345, third col., second paragraph) and peptides comprising this motif as regulators of cell proliferation. However, no in-vivo data are presented in D5 and D5 only states that the peptides comprising the mentioned motif can "decrease the rate of cell growth", (not induce programmed cell death), for which reason novelty is acknowledged in view of D5

Also D6 discloses that peptides comprising the present sequence (K/R)xxYDRxFL(L/M) can affect cell growth, (see D6 figure 1c and pages 1118-1119). However no in-vivo data are presented and D6 does not appear to explicitly teach programmed cell death. Thus, novelty appears to be acknowledgeable in view of D6.

V.2. Inventive step
Remarks under Article 33(3) PCT:

The common motif ((K/R)xxYDRxFL(L/M)), is already known, (see e.g. D5, page 345, third col., second paragraph, D6, the entire document, especially figure 1 and cf.

present application, page 3 lines 6-13). It appears further to have been shown in D4 that reducing the levels of eIF4E results in increased apoptosis of fibroblasts, (see D4, the entire document) and D5 teaches a clear role for eIF4E binding peptides in cell proliferation and even asks "by inhibiting eIF4E, might PHAS/4E-BP1 function as a tumor suppressor?", (see D5, page 349). Also D6 teaches a role of eIF4E binding peptides in cell proliferation, (see D6, page 1118, last paragraph - page 1119). Thus, it appears to be known already that peptides comprising the motif (K/R)xxYDRxFL(L/M) play a role in the regulation of proliferation of at least certain cell. D5 strongly suggests that inhibiting eIF4E by proteins comprising the motif (K/R)xxYDRxFL(L/M), (PHAS/4E-BP1) might lead to tumor suppression, (see D5, page 349, **PHAS/4E-BPs and cell proliferation**). Since "for induction of programmed cell death" according to present claim 1 is not a medical indication, but merely relates to a discovered property of the present motif, and the real medical indication must be assumed to be treatment of cancer/tumors, no inventive step can presently be acknowledged. In other words, even if a novel property of the present motif, (ability to induce cell death), is discovered no novel and inventive medical indication can be seen.

In this connection it is furthermore pointed out that the present application only appears to provide evidence that cell death is induced, when the cells are serum-deprived, (cf. pages 19-20). This does not appear to correlate with successful in-vivo treatment.

Section VIII

Remarks under Article 6 PCT:

Present claim 2 is unclear, because the latter two peptides mentioned do not appear to fall under the definition according to present claim 1.

CLAIMS

1. Use of a peptide comprising the sequence:

(K/R)XXYXXX(F/Q)L(L/M)

wherein x is a variable amino acid, in the manufacture of a medicament for the induction of programmed cell death.

2. Use according to claim 1 wherein said peptide comprises the sequence:

KKRYDREFLLGF,

RVRYSDQLLDL, or

RIIYDRKL(L/M).

3. Use according to claims 1 or 2 wherein said peptide is 7 - 25 amino acids in length.

4. Use of a peptide according to any of claims 1 to 3 wherein the medicament is used to induce cell death in tumour cells.

5. Use of a polynucleotide fragment encoding a peptide comprising sequence:

(K/R)XXYXXX(F/Q)L(L/M)

wherein x is a variable amino acid, in the manufacture of a medicament for the induction of programmed cell death.